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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,664	08/03/2005	Heinz-Josef Lenz	064189-0604	8635

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EXAMINER	
MYERS, CARLA J	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,664	LENZ ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,7-11,19,23,24,28-30 and 34-37* is/are pending in the application.

4a) Of the above claim(s) *7-11,29 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4, 19, 23, 24, 28, and 34-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/5/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 5, 2009 has been entered.

2. Applicant's amendments to the claims and arguments presented in the response of March 5, 2009 have been fully considered but are not persuasive to place all claims in condition for allowance.

All rejections not reiterated herein are hereby withdrawn.

In particular, the rejection of claims 1, 4 and 16-28 under 35 U.S.C. 112, first paragraph (enablement) is withdrawn in view of Applicant's arguments and amendments to the claims. It is noted that the post-filing date reference of Chang et al (Cancer Sci 2009. 100: 278-283; cited in the IDS of 3/5/09) teaches the results of a study of the ERCC1 codon 118 polymorphism in Asian metastatic colorectal cancer patients treated with 5-FU and oxaliplatin. Chang analyzed blood samples for the codon 118 polymorphism and found that the C/C genotype was associated with improved response rate, progression-free survival and long term survival (page 282, Table 3 and Figure 2). Ruzzo (Journal of Clinical Oncology. April 2007. 25: 1242-1254; cited in the IDS of 3/5/09) also teaches the results of a study of the ERCC1 codon 118

polymorphism in patients with metastatic colorectal cancer treated with 5-FU and oxaliplatin. Ruzzo analyzed blood samples from patients for the codon 118 polymorphism and found that the T/T genotype was associated with increased risk of progression (page 1248).

The rejection of claims 19-28 under 35 U.S.C. 112, second paragraph has been obviated by the amendments to the claims.

The provisional obviousness-type double patenting rejection has been obviated by the amendment to cancel the conflicting claims in application 11/173,889.

The rejection of claims 1,16-22, and 24-27 under 35 USC 103 over Park et al. and the rejection of claims 4, 23 and 28 under 35 U.S.C. 103(a) as being unpatentable over Park et al in view of Culy have been obviated by the amendment to the claims so that these claims are entitled to priority to application 60/400,253, filed July 31, 2002 and in view of the 132 Declaration of the present inventors.

Election/Restrictions

3. Claims 1, 4, 7-11, 19, 23, 24, 28, 29, 30, and 34-37 are pending.

Claims 7-11, 29 and 30 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 9, 2007.

In the reply of March 5, 2009, Applicants state that they traverse the withdrawal of claims 29-33 as being directed to non-elected subject matter. It is stated that claim 29

has been amended to recite "the steps of screening and identifying the patient for the same therapy as, for example, claims 1 and 19."

These arguments and the amendments to the claims have been fully considered but are not persuasive. Claim 29 has not in fact been amended to recite steps of screening and identifying the patient. Rather, claim 29 as amended recites "a patient selected for said therapy based on screening and the possession of the genotype (C/C) at codon 118 of the ERCC1 gene. This recitation does not constitute an active process step of screening a patient for the presence of a C/C genotype at codon 118 of the ERCC1 gene. Rather, the claim broadly recites that it is property of the patient that he/she has been screened – what the patient has been screened for is not recited. Further, the claim broadly recites that it is a property of the patient that they posses the genotype (C/C) at codon 118 of the ERCC1 gene. However, the fact that the patient has been screened and has a C/C genotype does not limit the claim methods which comprise screening for the C/C genotype (i.e., the subject matter of elected Group I). Therefore, claims 29 and 30 are directed to the subject matter distinct from that of the elected invention and are withdrawn from consideration.

It is noted that claims 29 and 30 would be rejoined with the elected claims if claims 29 and 30 were amended to recite an active process step of screening the nucleic acid sequence at codon 118 of the ERCC1 gene isolated from a sample obtained from the human metastatic colorectal cancer patient and determining that the patient has the C/C genotype at codon 118 of the ERCC1 gene.

Accordingly, claims 1, 4, 19, 24, 28 and 34-37 have been examined herein. Claims 7-11 and 29-30 are withdrawn from consideration as being drawn to a non-elected invention.

Claim Objections

4. A. Claims 36 and 37 are objected to because the claims depend from withdrawn claim 29.

B. Claim 24 recites "not having the genotype (C/T) or (T/T) genotype" whereas the claim should recite "not having the genotype (C/T) or (T/T)."

Declaration

5. The declaration under 37 CFR 1.132 filed March 5, 2009 is sufficient to overcome the rejection of claims 1,16-22, and 24-27 under 35 USC 103 over Park et al. and the rejection of claims 4, 23 and 28 under 35 U.S.C. 103(a) as being unpatentable over Park et al in view of Culy.

New Grounds of Rejection

Claim Rejections - 35 USC § 112 second paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4, 19, 23, 24, 28 and 34-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 4, and 34-37 are indefinite over the recitation of "the patient is not selected for the therapy." The claims are drawn to a method of selecting a therapy

rather than a method of selecting a patient. Accordingly, it is unclear as to how the limitation that the patient is not selected for therapy is intended to relate to the remainder of the claim. This rejection may be overcome by amendment of the claim to recite, for example, that the therapy is not selected for the patient if the patient has the C/T or T/T genotype at codon 118 of the ERCC1 gene.

Claims 19, 23, 24, 36 and 37 are indefinite over the recitation of "said therapy" and "the therapy" because these phrases lack proper antecedent basis. While the claims previously refer to "treatment," the claims do not previously refer to "therapy."

Priority

7. Claims 1, 4, 19, 23, 24, 28 , 34, 35 and 37 as amended in the response of March 5, 2009 are entitled to priority to provisional application 60/400,253 application, filed 7/13/02.

However, newly added claim 36 is entitled to priority only to PCT/US03/24065, filed July 31, 2003. Claims 36 is not entitled to priority to provisional applications 60/400,276, 60/400,250 or 60/400,249 because these applications do not provide support for the presently claimed invention of a method of selecting a therapy comprising 5-FU and oxaliplatin or determining if a human metastatic colorectal cancer is likely to experience longer survival by assaying for the presence of a C/C, C/T or T/T genotype at codon 118 of the ERRC1 gene.

Provisional application 60/400,253 application, filed 7/13/02 discloses a method of obtaining a nucleic acid sample from intratumoral tissue of a subject having metastatic colorectal cancer and assaying the nucleic acid sample to determine the

identity of the nucleotides in codon 118 to thereby detect the presence of codon AAC or AAT (e.g., page 2 and 25). The '253 application also provides support for the concept that the codon 118 C/C genotype is associated with associated with survival following 5-FU/oxaliplatin treatment, wherein patients having the C/C genotype survived for 531 days, patients with the C/T genotype survived for 254 days, and patients with the T/T genotype survived for 256 days (page 25). It is stated that the codon 118 polymorphism "maybe able to predict survival in patients with metastatic colorectal cancer treatment with 5-FU/oxaliplatin" (page 26). In particular, regarding claim 36, the '253 application discloses that the nucleic acid to be analyzed may be obtained from blood or from a patient tissue obtained from biopsies or resections (page 21). However, the '253 application does not appear to provide support for methods wherein the sample is normal tissue adjacent to the tumor or a peripheral blood lymphocyte. Note that the response of March 5, 2009 does not point to any particular teachings in the provisional applications as providing support for claim 36. It is also noted that a claim as a whole is assigned an effective filing date, rather than the subject matter within a claim being assigned individual effective filing dates. Accordingly, claim 36 is entitled only to the filing date of July 31, 2003.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 36 is rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al (Proceedings of the American Association for Cancer Research. March 2002. 43: 321, Abstract 1519 (cited in the IDS of May 15, 2008).

Park teaches a method of detecting the presence of the C or T polymorphism at codon 118 of the ERCC1 gene in intratumoral tissue samples from human subjects having metastatic colorectal cancer and treated with 5-FU/oxalipaltin. Park teaches that increased ERCC1 mRNA levels are directly related to clinical resistance to platinum chemotherapy. Park also teaches that the absence of the ERCC-1 C allele was associated with higher ERCC1 mRNA levels. The authors conclude that the codon 118 polymorphism “may potentially have a role [in] the prediction of clinical outcome in patients with metastatic colorectal cancer treated with 5-FU/oxaliplatin.”

Park does not specifically exemplify a method of selecting a patient for therapy with 5-FU/oxaliplatin by assaying for the presence of the C/C genotype at codon 118 or

predicting likelihood of longer survival by assaying for the presence of the C/C genotype at codon 118.

However, given the teachings of Park that increased ERCC1 mRNA levels are associated with resistance to treatment, and thereby with poorer response to treatment, and the teachings of Park that the C/C genotype is associated with decreased ERCC1 mRNA levels (while the T/T and C/T genotypes are associated with increased ERCC1 mRNA levels), and in view of the specific teachings of Park that the codon 118 polymorphism may be predictive of clinical outcome in metastatic colorectal cancer patients treated with 5-FU/oxaliplatin, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have applied the findings of Park to a method for selecting patients for 5-FU/oxaliplatin therapy and for predicting longer survival following 5-FU/oxaliplatin therapy. One would have been motivated to do so since Park teaches that the C/C genotype could be detected as indicative of susceptibility to 5-FU/oxaliplatin therapy, and thus longer survival following said therapy. Thereby, application of the method of Park to the selection of patients for 5-FU/oxaliplatin therapy and for predicting a patient's likelihood of longer survival following this therapy would have provided the expected benefit of ensuring the selection of the most effective therapy for patients having metastatic colorectal cancer. Application of the method of Park as set forth above would have resulted in a method of selecting metastatic colorectal cancer patients for 5-FU/oxaliplatin therapy and for predicting the likelihood that said patients will have a longer survival following therapy comprising screening a nucleic acid sequence at codon 118 of the ERCC1 gene

isolated from an intratumoral tissue sample of the patient for the genotype at codon 118 of the ERCC1 gene since Park teaches that it is the intratumor sample of the patient that is analyzed to determine the genotype at codon 118 of the ERCC1 gene.

Response to Remarks:

In the response, Applicants state that the Park et al reference was published less than one year prior to the effective filing date of July 13, 2002. It is stated that the previous rejection over Park et al has been obviated by the filing of the 132 Declaration establishing that the Park et al reference is not prior art to the claimed invention because the work described by Park et al is that of the present inventors.

However, for the reasons discussed above, claim 36 is not entitled to priority to the provisional applications having filing dates of July 13, 2002. Rather, claim 36 is entitled to priority only to PCT/US03/24065, filed July 31, 2003. Accordingly, the Park et al reference was published more than one year prior to the effective filing date of claim 36 and cannot be obviated by the 132 Declaration establishing that the Park reference is the work of the present inventors.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is 571-272-0747. The examiner can normally be reached on Monday-Thursday (6:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Carla Myers/

Primary Examiner, Art Unit 1634